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EXAMINER	
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ART UNIT	PAPER NUMBER
1647	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/518,956	HAJ ET AL.	
	Examiner	Art Unit	
	Ian Dang	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 May 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-12,15-19,21,24-40,43,45-56,59-64,66,68,69,71 and 152* is/are pending in the application.

4a) Of the above claim(s) *See Continuation Sheet* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *46, 49-50,59-64,68,69 and 71* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *17 December 2004* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *08/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

Continuation of Disposition of Claims: Claims withdrawn from consideration are 1-4,6-12,15-19,21,24-40,43,45,47,48,51-56,66 and 152.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

The amendment of 17 December 2004 has been entered in full. Claims 5, 13-14, 20, 22-23, 41-42, 44, 57-58, 65, 67, 70, 72-151, and 153 have been cancelled. Claims 1-4, 6-12, 15-19, 21, 24-40, 43, 45-56, 59-64, 66, 68, 69, 71, and 152 have been amended.

Election/Restrictions

Applicant's election with traverse of Group II, claims 46-56, 59-64, 68-69, and 71 in the communication filed on 05/08/2007 is acknowledged. The traversal is on the ground(s) there is no special technical feature over prior art because the reference by Cartmell et. al was published on or about March 8, 2003, which is after the June 19, 2002, the priority date of the present application.

Applicant's arguments filed 05/08/2007 have been fully considered but they are not persuasive. Although the Examiner agrees with Applicant that the reference by Cartmell et al. is not prior art to the instant application (see the declaration filed 05/08/2007), the instant application still does not form a single general inventive concept. At page 2 of the response Applicant indicates that the reference by Cartmell et al. is not prior art to the instant application because the reference by Cartmell et al. was published on March 8, 2003 and not June 2002 as indicated in the previous Office action. However, several prior art references meet the limitations of claim 1. For instance, Yanase et al. (1997, Japanese Journal of Cancer Research, Volume 88, Pages 630-632) teach a method of magnetically manipulating a cell comprising associating a magnetisable particle with a cell (page 630, Abstract) matching the limitations of claim 1. Thus Group I lacks novelty or inventive step and does not make a contribution over the

prior art. Since the first claimed invention has no special technical feature, it cannot share a special technical feature with the other claimed invention.

Under PCR Rule 13.1, the application shall relate to one invention only or to a group of inventions so linked as to form a single general inventive concept.

Claims 1-4, 6-12, 15-19, 21, 24-40, 43, 45, 47-48, 51-56, 66 and 152 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected non-invention, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8 May 2007. It is noted that claims 47-48 and 51-56 (which depend from claim 2) were erroneously included with Group II in the restriction requirement of 08 March 2007. Claims 47-48 and 51-56 should have been included with Group I. Hence, these claims are being withdrawn from consideration as being drawn to a non-elected invention.

Claims 46, 49-50, 59-64, 68-69, and 71 are pending and under examination.

Priority

Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file.

Claim Objections

Claims 49-50, 60 are objected to because of the following informalities:

Claim 60, line 2 is missing is missing a word or phrase after the term "cells".

Claim 49 recites the term "tumor" in line 2. Claim 50 (which depends from claim 49) recite the term "tumour" in line 2. While both spellings are correct, since claim 50 depends from claim 49, one spelling should be selected for consistency.

Claim Rejections - 35 USC § 112 (Written Description)

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 46, 49-50, 59-64, 68-69, and 71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claim 46 is drawn to a method of treating a patient suffering from a disorder involving an ion channel comprising administering the patient magnetisable particles, wherein the magnetisable particles associate with a cell of the patient; manipulating ion channels or cells using a magnetic field external to the patient thereby treating the disorder. In addition, claim 71 is drawn to method of administering to the patient a therapeutically active agent simultaneously, separately or sequentially with the magnetisable particle.

Specifically, the specification teaches that the method of treatment which is applicable to any disorder in which one or more ion channels play a role (page 8, line 25). In addition, the specification teaches that a wide variety of particles may be used in the method of the invention. The magnetisable particle used in the method of the invention may be inherently magnetic or, alternatively, may be one which reacts in a magnetic field. Generally any magnetic material

may be used, however, by the term magnetic we mean, for example, a material which is paramagnetic superparamagnetic, ferromagnetic and/or antiferromagnetic....(page 6 line 28 to page 7 to line 5). Finally, the specification teaches that channels are generally characterized by their ionic selectivity for example, sodium channel, potassium channel, calcium channel, chloride channel, non-selective cation channel (page 1 lines 16-21) and that more than 50 types of ion channels have been identified (page 1 lines 31-32).

Thus, the claims are genus claims. The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Specifically, the specification does not clearly define a disorder, an ion channel, magnetisable particles, a therapeutically active agent and all methods of using such. Thus, the scope of the claims includes numerous structural and functional variants, and the genus' are highly variant because a significant number of structural and functional differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural and functional features that could distinguish a disorder, an ion channel, magnetisable particles, and a therapeutically active agent are missing from the disclosure. No common attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, a disorder, an ion channel, magnetisable particles, and a therapeutically active agent are insufficient to describe the genus.

The written description requirement for a claimed genus' may be satisfied through sufficient description of a representative number of species by actual reduction to practice, reduction to drawings, or by disclosure of relevant identifying characteristics, i.e. structure or

other physical and/or chemical properties, by functional characteristics coupled with a known or disclosed correlation between structure and function structure, or by a combination of such identifying characteristics, sufficient to show the applicant was in possession of the claimed genus. In the instant case, the specification fails to provide sufficient descriptive information, such as definitive structural or functional features of the genus for a disorder, an ion channel, magnetisable particles, and a therapeutically active agent and all methods of using such.

There is no description of the special features, which are critical to the structure and function of the genus claimed. Furthermore, the prior art does not provide compensatory structural or correlative teachings sufficient to enable one of skill to isolate and identify a disorder, an ion channel, magnetisable particles, and a therapeutically active agent encompassed by the claims. Thus, no identifying characteristics or properties of a disorder, an ion channel, magnetisable particles, and a therapeutically active agent are provided such that one of skill would be able to predictably identify the encompassed variant biological and chemical entities recited in the methods of the instant claims. One of skill in the art would reasonably conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, applicant was not in possession of the claimed genus.

Claim Rejections - 35 USC § 112 (Enablement)

Claims 46, 49-50, 59-64, 68-69, and 71 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include: (1) Nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the breath of the claims, (7) the quantity of experimentation needed, (8) relative skill of those in the art.

Nature of the invention and breath of the claims

The invention is drawn to a method of treating a patient suffering from a disorder involving an ion channel comprising administering the patient magnetisable particles, wherein the magnetisable particles associate with a cell of the patient; manipulating ion channels or cells using a magnetic field external to the patient thereby treating the disorder. Claim 71 recites a method of administering to the patient a therapeutically active agent simultaneously, separately or sequentially with the magnetisable particle. The invention is broad because the method claims encompass a large number of disorders, ion channels, magnetisable particles, and active therapeutic agents.

Specifically, the specification teaches that the method of treatment which is applicable to any disorder in which one or more ion channels play a role (page 8, line 25). In addition, the specification teaches that a wide variety of particles may be used in the method of the invention. The magnetisable particle used in the method of the invention may be inherently magnetic or, alternatively, may be one which reacts in a magnetic field. Generally any magnetic material may be used, however, by the term magnetic we mean, for example, a material which is paramagnetic superparamagnetic, ferromagnetic and/or antiferromagnetic....(page 6 line 28 to page 7 to line 5). Finally, the specification teaches that channels are generally characterized by

their ionic selectivity for example, sodium channel, potassium channel, calcium channel, chloride channel, non-selective cation channel (page 1 lines 16-21) and that more than 50 types of ion channels have been identified (page 1 lines 31-32).

In addition, the association between the cell and the particles recited in claim 46 is broad. For instance the specification recites that the association of a magnetisable particle with a cell may comprise the introduction of such a particle into a cell, the attachment of such a particle to a cell, e.g. externally or internally to a cell, or any combination thereof (page 4, lines 4-6).

Unpredictability and state of the art

The state of the art for a method of treating a patient suffering from a tumor is well established, but treatment of any ion channel disorder comprising administering magnetisable particles to a patient wherein the particles target a cell of the patient and manipulating ion channels or cells using a magnetic fieldhas not been characterized at this point.

The injection of magnetizable particles for the treatment of tumor has been known for several years. For instance, Yanase et al. (1998, Japanese Journal of Cancer Research, Volume 89, pages 463-469) teach that the injection of magnetite cationic liposomes into tumors made up of soft glioma tissue and subjected to irradiation by an alternating magnetic field resulting into tumor regression (page 463, abstract).

However, the role of ion channels as a target for the treatment of a disorder, such as cancer, has not been established at the present time. There are numerous uncertainties regarding the role of ion channels for the development of cancer. For instance, Kunzelman 2005) recites that considerable evidence exists for the contribution of ion channels to development and growth of cancer and malignancy of the tumor, yet a clinical application of this knowledge appears to be far away. Some of the reasons include the incomplete understanding

of K+ channels and other ion channels for cell proliferation and apoptosis and little knowledge regarding the functional impact of the channel in the real tissue and the role of these channels at different stages of tumor development (page 168, right column, 2nd paragraph).

In addition, the state of the art teaches that magnetizable particles may potentially be used in numerous diagnostic and therapeutic applications. For instance, in recent review article, Ito et al., (2005) teach that magnetic nanoparticles can be used in several applications, such as magnetic separation, cancer diagnosis (MRI), hyperthermia and tissue engineering (page 8, right column, last paragraph).

Furthermore, the state of the art regarding the role of ion channels in tissue/bone repair, tissue generation, wound healing/tissue adhesion has not been completely established because understanding their activities require further experiments. For instance, O'Grady et al., (2005) recite that certain ion channels, such the voltage gated potassium channels on epithelial cells may be involved in cell migration and wound healing, cell proliferation and cancer, apoptosis and O2 sensing (page 1578, abstract). However, O'Grady et al., further teach that further studies exploring the mechanisms of proliferation, differentiation, apoptosis, and oxidant injury will likely provide important insights into functions of voltage-gated K+ channels in physiology of epithelial cells (page 1590, left column, last paragraph).

In addition, the state of the art regarding the role of ion channels in bone metabolism is still not predictable. For instance, Komarova et al. (2001) teach that ion channels on osteoclasts can be a potential target for antiresorptive drugs. It is conceivable that agents will be identified that target specifically to bone or interact selectively with osteoclast ion channels to inhibit resorption in metabolic and inflammatory bone diseases (page 651, right column bottom of last paragraph).

While the art provides limited experimental evidence for the role of ion channels in wound healing and in bone repair, the specification does not provide any link, connection, or evidence that magenisable particles can be used in a method for the treatment of a tissue/bone repair, tissue generation, wound healing/tissue adhesion as recited in claims 59-64.

Although the specification of the instant application discloses in vitro examples utilizing the potassium channel, TREK-1, TREK-1 is a single type of ion channel among more than 50 types of ion channels that have been identified (page 1 lines 31-32). Each ion channel has distinct structure and function. As disclosed in the specification (page 1, lines 15-23), a channel's functional properties depend on their ionic selectivities. Thus, one skilled in the art would not be able to predict that TREK-1 is representative for all ion channels or that TREK-1 can be used as a therapeutic target for the treatment of any disorders.

In view of these teachings in the art and the limited guidance provided in the specification (the interactions of magnetisable particles with TREK-1 in vitro (examples 1-3)), one skilled in the art would not be able to predict that administering magnetisable particles would treat a patient suffering from a disorder involving an ion channel.

The amount of direction or guidance present

Applicants' disclosure is limited to the study for the interactions of magnetizable particles with TREK-1 in vitro. The specification discloses examples of associating magnetisable particles with TREK-1 in vitro, activation of TREK-1 using magnetic cytometry (Example 1), deformation of membrane using magnetic cytometry (Example 2, page 17), and intracellular calcium activity of TREK-1 (Examples 3 and 4 page 18).

However, the specification does not provide guidance or direction regarding other ion channels besides TREK-1, any disorder associated with any ion channels, the identifying characteristics for the ion channels needed for treatment, the concentrations of magnetisable

particles, or the length of time of the treatment with the magnetisable particles. In addition, one skilled in the art would not be able to predict that administration of possible magnetisable particles can treat all possible ion channel disorders. Applicant has not provided guidance for any disorder involving an ion channel and how the interaction between a magnetic particle and an ion channel can lead to treatment of the disorder. There is also little guidance provided in the specification as to how the magnetic particles would target the appropriate cells in the patient.

Applicant has not provided sufficient guidance regarding the magnetisable particles. The specification teaches that the magnetisable particles used in the method of the invention may be inherently magnetic or, alternatively, may be one which reacts in a magnetic field. Generally any magnetic material may be used, however, by the term magnetic we mean, for example, a material which is paramagnetic superparamagnetic, ferromagnetic and/or antiferromagnetic....(page 6 line 28 to page 7 to line 5). Furthermore, the specification and the claims have not provided sufficient evidence for identifying the patient population needed for a method of treating a patient suffering from a disorder involving an ion channel. The patient population is not well defined for the claimed invention because it includes any patient.

Working Examples

Although Applicants have provided examples magnetisable particles associating with TREK-1 in vitro, such as activation of TREK-1 using magnetic cytometry (Example 1), deformation of membrane using magnetic cytometry (Example 2, page 17), and intracellular calcium activity of TREK-1 (Examples 3 and 4 page 18), the specification does not provide any methods or working examples for administering the particles in an animal model or in patients.

The specification also does not provide any methods or working examples for the treatment of any specific disorder involving any ion channels with magnetisable particles.

The quantity of experimentation needed

Without sufficient disclosure in the specification, it would require undue experimentation for one of skill in the art to be able to treat a patient suffering from any disorder involving an ion channel comprising administering patients with magnetisable particles.

In addition, it would require undue experimentation to practice the invention commensurate in scope with the claims because, the claims are broadly drawn to a method of treating a patient suffering from a disorder involving an ion channel comprising administering the patient magnetisable particles, wherein the magnetisable particles associate with a cell of the patient; manipulating ion channels or cells using a magnetic field external to the patient thereby treating the disorder.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 46, 49-50, 59-64, 68-69, and 71 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

(a) Claims 59-64 are indefinite because the elements recited in the claims do not constitute proper Markush groups. The claims are indefinite in the alternative use of "and/or" because it is not clear what controls which of these limitations. (See especially claims 59, 63, and 64.) See MPEP § 2173.05(h).

(b) Claims 46, 49-50, 59-64, 68-69, 71 are rejected as being indefinite because Claim 46, line 6 recites the limitation "ion channels". There is insufficient antecedent basis for this limitation in the claim. It is not clear what ion channels are being referred to in the claim.

(c) Claims 59-64 are rejected as being indefinite because it is not clear how they depend from claim 46. For instance, claim 46 recites a method of treating a patient suffering from a disorder involving an ion channel. However, claims 59-64 recite, for example, "[t]he method of claim 46 wherein the method is a method of tissue and/or bone repair". (Please note that this issue could be overcome, by amending the claims to recite, for example, "...the method of claim 46 wherein the disorder requires tissue and/or bone repair".)

(d) Claims 46, 49-50, 59-64, 68-69, 71 are rejected as being indefinite because Claim 46, recites the limitation "manipulating". The term "manipulating" in claim 46 is a relative term which renders the claim indefinite. The term "manipulating" is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the scope of the invention. For instance, it is unclear to what is encompassed by the term "manipulating".

(e) Claim 50 is are rejected as being indefinite because Claim 46, line 6 recites the limitation "tumor cell" and "cancer cell". The meaning of both phrases encompasses the same type of cell. It is unclear how these two phrases are different from each other.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim 46 is rejected under 35 U.S.C. 102(b) as being anticipated by Yanase et al. (1998, Japanese Journal of Cancer Research, Volume 89, pages 463-469).

Yanase et al. (1998,) teach that the injection of magnetite cationic liposomes into tumors made up of soft glioma tissue and subjected to irradiation by an alternating magnetic field resulting into tumor regression (page 463, abstract) meeting the limitations of claims 46 and 47. Although the reference by Yanase et al. do not explicitly teach a disorder involving an ion channel, Ullrich et al. (1998; Neuroscience, Volume 83, Issue 4, pages 1161-1173) teach that the expression of chloride channels in human gliomas is probably a glioma-specific feature (Page 1161, last line of abstract).

Conclusion

No claim is allowed.

Information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Ian Dang whose telephone number is (571) 272-5014. The examiner can normally be reached on Monday-Friday from 9am to 5pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Nickol can be reached on (571) 272-0835. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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